

CP the right ITR. Furthermore, the pBr/Ad.BamRfib 12 and pBr/Ad.BamRfib 28 contain an internal BamHI site in the fiber sequences and were therefor digested with SalI which cuts in the vector sequences flanking the BamHI site. For transfection, 2 μ g of pCLIPsal-Luc, and 4 μ g of both pWE/Ad.AflII-Eco and pBr/AdBamR.pac/fibXX were diluted in serum free DMEM to 100 μ l total volume. To this DNA suspension 100 μ l 2.5x diluted lipofectamine (Gibco) in serum-free medium was added. After 30 minutes at room temperature the DNA-lipofectamine complex solution was added to 2.5 ml of serum-free DMEM which was subsequently added to a T25 cm² tissue culture flask. This flask contained PER.C6 cells that were seeded 24-hours prior to transfection at a density of 1×10^6 cells/flask. Two hours later, the DNA-lipofectamine complex containing medium was diluted once by the addition of 2.5 ml DMEM supplemented with 20% fetal calf serum. Agains 24 hours later the medium was replaced by fresh DMEM supplemented with 10% fetal calf serum. Cells were cultured for 6-8 days, subsequently harvested, and freeze/thawed 3 times. Cellular debris was removed by centrifugation for 5 minutes at 3000/rpm room temperature. Of the supernatant (12.5 ml) 3-5 ml was used to infect again PER.C6 cells (T80 cm² tissue culture flasks). This re-infection results in full cytopathogenic effect (CPE) after 5-6 days after which the adenovirus is harvested as described above.

IN THE CLAIMS:

CP 1. (Thrice amended) A gene delivery vehicle comprising a tissue tropism determining fragment of a subgroup B adenovirus fiber protein, wherein the tissue tropism determining fragment exhibits at least a tissue tropism for smooth muscle cells.

CP 2. 4. (Amended) The gene delivery vehicle of claim 1 wherein said tissue tropism determining fragment is provided by a virus capsid.

P. 16 F17
C 11
19. (Thrice amended) A cell for producing a gene delivery vehicle having a tissue tropism for smooth muscle cells said cell comprising means for the assembly of gene delivery vectors wherein said means includes at least one adenovirus nucleic acid for the production of an adenoviral fiber protein, wherein said adenoviral fiber protein comprises at least a tissue tropism determining fragment of a subgroup B adenoviral fiber protein.

20. (Thrice amended) The cell of claim 19, wherein said cell is of PER.C6 (ECACC deposit number 96022940) origin.

24. (Thrice amended) An adenovirus capsid having a tissue tropism for smooth muscle cells wherein said capsid comprises proteins from at least two different adenoviruses and wherein at least a tissue tropism determining fragment of a fiber protein is of subgroup B adenovirus origin.

8 F17
C 12
25. (Thrice amended) An adenovirus capsid with a significantly reduced tissue tropism for liver cells wherein said adenovirus capsid comprises proteins from at least two different adenoviruses and wherein at least a tissue tropism determining fragment of a fiber protein is of subgroup B adenovirus origin.

26. (Thrice amended) A method of delivering nucleic acid to smooth muscle cells, said method comprising:
administering to said smooth muscle cells a gene delivery vehicle comprising an adenovirus capsid comprising proteins from at least two different adenoviruses and wherein at least a tissue tropism determining fragment of a fiber protein is of subgroup B adenovirus origin.

C 3
P. 16 F17
28. (Amended) A construct deposited with the ECACC under deposit number 01121708 on December 12, 2001.

29. (Amended) A construct deposited with the ECACC under deposit number 01121710 on December 12, 2001.

30. (Amended) A construct deposited with the ECACC under deposit number 01121709 on December 12, 2001.

Q13 31. (Amended) A construct deposited with the ECACC under deposit number 01121711 on December 12, 2001.

32. (Amended) A construct deposited with the ECACC under deposit number 0112712 on December 12, 2001.

Q14 37. (Thrice amended) A method of reducing an adenovirus capsid of a tissue tropism for liver cells, said method comprising incorporating a fragment of a fiber protein of adenovirus 16 in an adenovirus capsid therefor.

Q15 44. (Amended) A gene delivery vehicle comprising increased tissue tropism for endothelial cells when compared to other gene delivery vehicles, wherein said tissue tropism is being provided by a virus capsid and wherein said virus capsid comprises protein fragments from at least two different viruses.

Q16 47. (Amended) The gene delivery vehicle of claim 44 wherein at least one of said protein fragments comprises a tissue tropism determining fragment of a fiber protein of subgroup B adenovirus origin.

Q17 49. (Amended) The gene delivery vehicle of claim 44 wherein said protein fragments are not from an adenovirus of subgroup B and are of adenovirus of subgroup C origin.

~~Q19~~ ~~ant #17~~ 52. (Amended) The gene delivery vehicle of claim 51 wherein said adenoviral nucleic acid comprises sequences from at least two different adenoviruses.

~~Q19~~ ~~ant #17~~ 58. (Amended) An adenovirus capsid having an increased tissue tropism for endothelial cells when compared to other adenovirus capsids, wherein said capsid comprises proteins from at least two different adenoviruses and wherein at least a tissue tropism determining fragment of a fiber protein is of subgroup B adenovirus origin.